PHARMACY COVERAGE GUIDELINE

IRON CHELATING AGENTS:
Deferasirox tab for oral suspension
Deferasirox oral granules
Deferiprone oral tab
EXJADE (deferasirox) tab for oral suspension
FERRIPROX (deferiprone) oral tab
FERRIPROX (deferiprone) oral solution
JADENU (deferasirox) oral tab
JADENU Sprinkle (deferasirox) oral granules

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

Deferasirox tab for oral suspension
Deferasirox oral granules
EXJADE (deferasirox) tab for oral suspension

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JADENU (deferasirox) oral tab
JADENU Sprinkle (deferasirox) oral granules

- **Criteria for initial therapy:** Exjade tab for oral suspension, Jadenu oral tab, Jadenu Sprinkle oral granules, deferasirox tab for oral suspension, or deferasirox oral granules is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Hematologist or Oncologist

2. Individual has a confirmed diagnosis of **chronic iron overload** due to **ONE** of the following:
    a. Transfusional hemosiderosis in an individual 2 years of age or older with **ALL** of the following:
        i. Evidence of transfusion related iron overload that includes **ONE** of the following:
            1. Transfusion with at least 100 mL/kg of packed red blood cells (PRBC) (e.g., at least 20 units of PRBC for a 40 kg person or more in individuals weighing more than 40 kg)
            2. A history of frequent blood transfusions that have resulted in chronic iron overload
        ii. Serum ferritin consistently greater than 1,000 mcg/L

    b. Non-transfusional thalassemia (NTDT) syndromes in an individual 10 years of age or older with **ALL** of the following:
        i. Serum ferritin consistently greater than 300 mcg/L on at least 2 measurements at least one month apart
        ii. Liver iron concentration (LIC) is at least 5 mg iron/g of liver dry weight by biopsy **or** by an alternative FDA-cleared or approved method

    c. Myelodysplastic syndromes (MDS) in an individual who is at low risk or intermediate-1 risk or a potential transplant and has received or is anticipated to receive greater than 20 red blood cell transfusions and MRI or a liver biopsy suggests substantial liver iron overload

3. Individual has completed **ALL** the following **baseline tests** before initiation of treatment and will have continued monitoring as clinically appropriate:
    a. Serum ferritin
    b. Serum transaminases and bilirubin
    c. Serum creatinine is measured in duplicate
    d. Estimated glomerular filtration rate (eGFR) by CKD-EPI or MDRD method in adults; by Schwartz equation in pediatric individual
    e. Urinalysis and serum electrolytes
    f. Auditory examination
    g. Ophthalmic examination including slit lamp examination and dilated fundoscopy
    h. When used for iron overload in low-risk myelodysplastic syndrome (MDS), **ALL** of the following:
        i. IPSS or IPSS-R score (score must be submitted with request)
        ii. Performance status (score must be submitted with request) using **ONE** of the following:
            1. Eastern Cooperative Oncology Group (ECOG) Performance score
            2. Karnofsky score **or** for age 10 years or less a Lansky Play score

4. There are **NO** FDA-label contraindications such as:

a. Estimated glomerular filtration rate (eGFR) less than 40 mL/min/1.73 m^2
b. Individual with a platelet count of less than 50 x 10^9/L
c. Individual with high-risk myelodysplastic syndrome (MDS) defined by either IPSS or IPSS-R
d. Individuals with advanced malignancies
e. Known hypersensitivity to deferasirox or any component
f. Individual with poor performance status defined by **ONE** of the following:
    i. ECOG score ≥ 3 **or**
    ii. Karnofsky score < 70% **or**
    iii. For age ≤ 10: Lansky Play < 70%

5. **For brand Exjade tab oral suspension only:** Individual has failure after adequate trial (for at least 3 months), contraindication per FDA label, intolerance, or is not a candidate for **generic deferasirox tab oral suspension** (generic for Exjade) (see Definitions section)

6. **For brand Jadenu oral tab or deferasirox oral granules products:** Individual has failure after adequate trial (for at least 3 months), contraindication per FDA label, intolerance, or is not a candidate for the **generic deferasirox oral tab** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

7. **For brand Jadenu Sprinkle oral granules only:** Individual has failure after adequate trial (for at least 3 months), contraindication per FDA label, intolerance, or is not a candidate for **BOTH** of the following (see Definitions section):
    a. Deferasirox oral tab (generic for Jadenu)
    b. Deferasirox oral granules packet (generic for Jadenu Sprinkle)

8. Will not be used in individuals with severe hepatic impairment (Child-Pugh Class C)

9. Will not be used in combination with other iron chelation therapies

10. Individual is not currently taking any other drugs which cause severe adverse reactions or any drug interactions requiring discontinuation such as aluminum containing antacids, theophylline, tizanidine, and potent UGT inducers such as rifampicin, phenytoin, phenobarbital, ritonavir

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Exjade tab for oral suspension, Jadenu oral tab, Jadenu Sprinkle oral granules, deferasirox tab for oral suspension, or deferasirox oral granules is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Hematologist or Oncologist

2. Individual has documentation of positive clinical response to therapy defined as the following:
    a. **For transfusional hemosiderosis**:
        i. Serum ferritin decreased over baseline but is still > 500 mcg/L, if ferritin is consistently < 500 mcg/L, deferasirox must be discontinued
        ii. Platelet count is greater than 50 x 10^9/L

iii. eGFR is greater than 40 mL/min/1.73 m^2

b. **For NTDT**: (if a serum ferritin and LIC is submitted, the LIC is used for determination)
   i. Serum ferritin decreased over baseline but is still > 300 mcg/L, if ferritin is consistently < 300 mcg/L, deferasirox must be discontinued
   ii. LIC decreased over baseline but is still ≥ 5 mg Fe/g dw, if LIC is consistently < 3 mg Fe/g dw, deferasirox must be discontinued
   iii. Platelet count is greater than 50 x 10^9/L
   iv. eGFR is greater than 40 mL/min/1.73 m^2

c. **For MDS**:
   i. Achieved and maintains a serum ferritin level of less than 1,000 ng/mL
   ii. eGFR is greater than 40 mL/min/1.73 m^2

3. **For brand Exjade tab oral suspension only:** Individual has failure after adequate trial (for at least 3 months), contraindication per FDA label, intolerance, or is not a candidate for **generic deferasirox tab oral suspension** (generic for Exjade) [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

4. **For brand Jadenu oral tab:** Individual has failure after adequate trial (for at least 3 months), contraindication per FDA label, intolerance, or is not a candidate for the **generic deferasirox oral tab** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. **For brand Jadenu Sprinkle oral granules only:** Individual has failure after adequate trial (for at least 3 months), contraindication per FDA label, intolerance, or is not a candidate for **deferasirox oral granules** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual has been adherent with the medication

7. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use as follows:
   a. Contraindications as listed in the criteria for initial therapy section
   b. Significant adverse effect such as:
      i. Severe cutaneous adverse reactions (SCARs) including Stevens Johnson syndrome, toxic epidermal necrolysis, erythema multiforme, or drug reaction with eosinophilia and systemic symptoms (DRESS)
      ii. Acute renal injury, including acute renal failure requiring dialysis and renal tubular toxicity including Fanconi syndrome
      iii. Hepatic toxicity
      iv. GI bleeding, ulceration, or perforation
      v. Bone marrow suppression such as neutropenia, agranulocytosis, worsening anemia, and thrombocytopenia
      vi. Severe auditory abnormalities
      vii. Severe ocular abnormalities

8. Will not be used in individuals with severe hepatic impairment (Child-Pugh Class C)

9. Will not be used in combination with other iron chelation therapies

10. Individual is not currently taking any other drugs which cause severe adverse reactions or any drug interactions requiring discontinuation such as aluminum containing antacids, theophylline, tizanidine, and potent UGT inducers such as rifampicin, phenytoin, phenobarbital, ritonavir

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**
2. **Off-Label Use of Cancer Medications**

Deferiprone oral tab
FERRIPROX (deferiprone) oral tab
FERRIPROX (deferiprone) oral solution

- **Criteria for initial therapy:** Ferriprox (deferiprone) oral tab, Ferriprox (deferiprone) oral solution, or generic deferiprone oral tab is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's condition or is in consultation with a Hematologist or Oncologist
2. Age of the individual is consistent with product formulation as per FDA label is **ONE** of the following:
    a. Oral tablet 8 years of age or older
    b. Oral solution: 3 years of age or older
3. Individual has a confirmed diagnosis of **transfusional iron overload** due to **ONE** of the following:
    a. Thalassemia syndromes with serum ferritin levels that are consistently > 2,500 mcg/L with previous iron chelation therapy
    b. Sickle Cell Disease or other transfusion-dependent anemias with serum ferritin level of at least 1,000 mcg/L or liver iron concentration of at least 3 mg/g dry weight by biopsy or by an alternative FDA-cleared or approved method
4. Individual does not have transfusional iron overload due to Myelodysplastic Syndrome (MDS) or Diamond Blackfan anemia
5. **For brand Ferriprox (deferiprone) oral tab and Ferriprox (deferiprone) oral solution**: Individual has a documented failure (for at least 3 months), contraindication per FDA label, intolerance, or is not a candidate for **generic deferiprone oral tab** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual has completed **ALL** the following **baseline tests** before initiation of treatment and will have continued monitoring as clinically appropriate:
    a. Absolute neutrophil count is greater than 1.5 x 10^9/L
    b. Hepatic transaminase levels
    c. Zinc levels
    d. Negative pregnancy test in a woman of childbearing potential

7. Will not be used in individuals with severe hepatic impairment (Child-Pugh Class C)

8. Will not be used in individuals with end stage renal disease (eGFR less than 15mL/min/1.73m^2)

9. Will not be used in combination with other iron chelation therapies

10. There are no significant interacting drugs, UGT1A6 inhibitors such as diclofenac, phenylbutazone, probenecid, silymarin (milk thistle)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Ferriprox (deferiprone) oral tab, Ferriprox (deferiprone) oral solution, or generic deferiprone oral tab is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met: **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's condition or is in consultation with a Hematologist or Oncologist

2. Individual has documentation of positive clinical response to therapy defined as **ONE** of the following:
    a. Serum ferritin decreased by at least 20% over baseline but is still > 500 mcg/L, if ferritin is consistently less than 500 mcg/L, deferiprone must be discontinued
    b. Liver iron concentration (LIC) decreased over baseline

3. **For brand Ferriprox (deferiprone) oral tab**: Individual has failure (for at least 3 months), contraindication per FDA label, intolerance, or is not a candidate for **generic deferiprone oral tab** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

4. **If available: For brand Ferriprox (deferiprone) oral solution**: Individual has failure (for at least 3 months), contraindication per FDA label, intolerance, or is not a candidate for **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Absolute neutrophil count is greater than 1.5 x 10^9/L

6. Individual has been adherent with the medication

7. Individual has not developed any significant adverse drug effects that may exclude continued use such as:
    a. Agranulocytosis/neutropenia

b. Hepatic impairment with liver enzymes that are persistently elevated

8. Will not be used in individuals with severe hepatic impairment (Child-Pugh Class C)
9. Will not be used in individuals with end stage renal disease (eGFR less than 15mL/min/1.73m^2)
10. Will not be used in combination with other iron chelation therapies
11. There are no significant interacting drugs, UGT1A6 inhibitors such as diclofenac, phenylbutazone, probenecid, silymarin (milk thistle)

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**
2. **Off-Label Use of Cancer Medications**

Description:

Deferasirox (Exjade, Jadenu & Jadenu Sprinkles) are indicated for the treatment of chronic iron (Fe) overload in patients 2 years of age and older whose iron overload is due to blood transfusions (transfusional hemosiderosis) who received at least 100 mL/kg of packed red blood cells and have a serum ferritin that is consistently greater than 1,000 mcg/L. It is also indicated for the treatment of chronic iron overload in patients 10 years of age and older with non-transfusion-dependent thalassemia (NTDT) syndromes with liver iron concentration (LIC) of at least 5 milligrams of iron per gram of liver dry weight (mg Fe/g dw) and a serum ferritin greater than 300 mcg/L. The safety and efficacy of deferasirox in combination with other iron chelation therapies have not been established.

Deferiprone (Ferriprox) is another oral iron chelating agent indicated for the treatment of patients transfusional iron overload in adults and pediatric patients ≥ 8 years of age (tablets) or adults and pediatric patients ≥ 3 years of age (oral solution) with thalassemia syndromes, sickle cell disease, or other anemias. The safety and effectiveness of deferiprone have not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome or Diamond Blackfan anemia. Ferriprox tablets are available in three formulations. There are *two different 1,000 mg formulations*, and a 500 mg formulation, which have different dosing regimens to achieve the same total daily dosage. One 1,000 mg tablet formulation is dosed twice a day while the other 1,000 mg tablet is dosed three times a day. The 500 mg tablet is dosed three times a day.

An injectable iron chelating agent, deferoxamine (Desferal and generics), is available and is administered intramuscularly, subcutaneously, or intravenously. It is indicated for the treatment of acute iron intoxication and of chronic iron overload due to transfusion-dependent anemias.

All body cells need iron. t is crucial for oxygen transport, energy production, and cellular growth and proliferation. The human body contains an average of 3.5 g of iron (males 4 g, females 3 g).

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Iron is bound and transported in the body by the glycoprotein carrier protein transferrin, and it is stored in ferritin molecules. Ferritin is particularly abundant in the liver and heart. When there is an excess of iron, the body responds by producing more ferritin to facilitate iron storage. When there is an excess of iron, the body responds by producing more ferritin to facilitate the iron storage. When iron concentrations exceed the storage capacity of ferritin molecules, unbound iron deposits in many organs and causes free-radical formation in cells, resulting in membrane lipid peroxidation, cellular injury, and organ dysfunction. Iron overload may result from either inherited or acquired disorders such as transfusion dependent anemia, various liver diseases, hemolytic anemia, thalassemia, sickle cell anemia and excessive iron ingestion.

Determination of iron status can be accomplished by several methods. Serial measurement of serum ferritin is a reliable and the easiest method to evaluate iron overload. Elevated serum ferritin is a sensitive test for iron overload, but it is not very specific. The normal range for ferritin in plasma or serum is approximately 40-200 mcg/L (40-200 ng/mL; 89.9-449.4 picomoles/L). A ferritin level ≥ 200 to 300 mcg/L in a man (or ≥ 150 to 200 mcg/L in a woman) is consistent with iron overload, and a level below these values is good evidence that the patient does not have iron overload. Ferritin levels in iron overload may range of up to 2000 to 3000 mcg/L (ng/mL).

Determination of liver iron concentration (LIC) can be done via a liver biopsy, but it is an invasive procedure with the possibility of complications. Nuclear magnetic resonance imaging techniques for assessing total body iron is available.

LIC estimates by MRI > 2-7 mg Fe/g dry weight (equivalent to approximately 53-125 micromol/g dry weight) indicates the presence of hepatic iron overload. A cardiac T2* by MRI of less than 20 milliseconds (normal is less than 20) indicates the presence of cardiac iron overload. Values of less than 10 milliseconds have been associated with severe myocardial iron loading and the development of cardiac failure.

Myelodysplastic syndrome (MDS) refers to a heterogeneous group of clonal hematopoietic disorders with the potential to transform into acute myelocytic leukemia (AML). Anemia is often seen and may require red blood cell (RBC) transfusions and subsequent iron overload. Guidelines suggest the use of iron chelating agents in patients with MDS and iron overload, although the benefit of iron chelation in MDS is unproven and the optimal agent to use is unclear at this time.

Prophylactic or therapeutic iron chelation treatment is suggested for low risk MDS who have had, or are anticipated to have, prolonged red cell transfusion requirements (more than 20-30 transfusions), demonstrate evidence of iron overload (serum ferritin >1000 mcg/L), the LIC is > 3 mg Fe/g dry weight, and/or the cardiac T2* is <20 milliseconds.

The International Prognostic Scoring System (IPSS) and a revised IPSS (IPSS-R) use cytogenetic, morphologic, and clinical data to define MDS risk groups. IPSS for MDS stratifies patients into four distinctive risk groups in terms of both survival and AML evolution. The IPSS-R defines five risk groups.

The latest National Comprehensive Cancer Network (NCCN) Guidelines Clinical Practice Guidelines in Oncology: Myelodysplastic Syndromes (Version 3.2024, Jul 25, 2024) states iron chelation therapy to decrease iron overload, should be considered if > 20-30 RBC transfusions have been given, particularly for patients who have lower-risk MDS or who are potential transplant candidates (LOW/INT-1). It also states that the aim is to decrease ferritin levels to < 1,000ng/mL for patients with serum ferritin levels > 2,500ng/mL.

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Definitions:

Deferasirox Oral

Exjade tab for suspension and generic tab for suspension:125mg, 250mg, 500mg
Jadenu tab and generic tab: 90mg, 180mg, 360mg:
Jadenu Sprinkle granules and generic sprinkle granules: 90mg, 180mg, 360mg

Deferiprone Oral

Ferriprox Twice-A-Day tab 1,000mg
Ferriprox Three-A-Day tab 1,000mg
Ferriprox Three-A-Day tab 500mg
Deferiprone generic Three-A-Day tab 500mg
Ferriprox oral solution 100mg/mL, 500mL

Brands	Strengths	Generics
Exjade (deferasirox) tab for oral suspension	125 mg, 250 mg, 500 mg	Deferasirox tab for oral suspension
Jadenu (deferasirox) oral tab	90 mg, 180 mg, 360 mg	Deferasirox oral tab
Jadenu Sprinkle (deferasirox) oral granules	90 mg, 180 mg, 360 mg	Deferasirox oral granules
Ferriprox (deferiprone) oral tab		
Twice-A-Day tab	1,000mg	None
Three-A-Day tab	1,000mg	Deferiprone oral tab
Three-A-Day tab	500mg	Deferiprone oral tab
Ferriprox (deferiprone) oral solution	100 mg/mL (50 g/500 mL)	None

Deferasirox Oral

Indications

- **Chronic iron overload due to blood transfusions**
  - Treatment of chronic iron overload caused by blood transfusions (transfusional hemosiderosis) in patients ≥ 2 years of age
- **Chronic iron overload in non-transfusion-dependent thalassemia syndromes**
  - Treatment of chronic iron overload in patients ≥ 10 years of age with non-transfusion-dependent thalassemia syndromes and with a liver iron concentration of at least 5 mg of iron per gram of liver dry weight (mg Fe/g dry weight) and a serum ferritin > 300 mcg/L

Limitations of use

- Safety and efficacy of deferasirox in combination with other iron chelation therapies have not been established

Deferiprone Oral

Indications

- **Transfusional iron overload**
  - Treatment of transfusional iron overload in adults and pediatric patients ≥ 8 years of age (tablets) or adults and pediatric patients ≥ 3 years of age (oral solution) with thalassemia syndromes, sickle cell disease, or other anemias

Limitation of use

- Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome or Diamond Blackfan anemia

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The Child-Pugh classification system: A scoring system used to determine the prognosis of individuals with cirrhosis. Scoring is based upon several factors: albumin, ascites, total bilirubin, prothrombin time, and encephalopathy, as follows:

	Score: 1 point	Score: 2 points	Score: 3 points
Serum Albumin (g/dL)	>3.5	3.0 - 3.5	<3.0
Serum Bilirubin (mg/dL)	<2.0	2.0 - 3.0	>3.0
Prothrombin time (seconds)	1 - 4	4 - 6	>6
Ascites	none	moderate	severe
Encephalopathy	none	mild	severe

The three classes and their scores are:

- **Class A** is score 5 – 6: Well compensated
- **Class B** is score 7 – 9: Significant functional compromise
- **Class C** is score >9: Decompensated disease

Methods for measuring iron overload:

Liver iron concentration (LIC) by biopsy
Magnetic resonance imaging with R2* or T2*
R2 technique

Thalassemia syndromes:

Alpha-thalassemia silent carrier	Mild Hb-E / Beta-thalassemia
Alpha-thalassemia trait (minor)	Moderately severe Hb-E / Beta-thalassemia
Hemoglobin H disease	Severe Hb-E / Beta-thalassemia
Hemoglobin Bart's Hydrops fetalis syndrome	Delta-thalassemia
Beta-thalassemia trait (minor)	Hemoglobin S thalassemia
Thalassemia intermedia	Hemoglobin C thalassemia
Beta-thalassemia major (Cooley's anemia)	Hemoglobin D thalassemia
Beta-thalassemia minor	Delta-thalassemia
Hemoglobin E (Hb-E) thalassemia	Hereditary persistence of fetal hemoglobin (HPFH)

Myelodysplastic syndrome (MDS):

A heterogeneous group of clonal hematopoietic disorders with the potential to transform into acute myelocytic leukemia (AML). MDS include, *but are not limited to:*

- del 5q syndrome
- Refractory anemia
- Refractory anemia with:
  - Ringed sideroblasts
  - Excess blasts 1 and 2
- Refractory cytopenia with multilineage dysplasia or ring sideroblasts

International Prognostic Scoring System for MDS:

International Prognostic Scoring System (IPSS)					
Survival and AML evolution					
	Score value				
Prognostic variable	0	0.5	1	1.5	2
Bone marrow blasts (%)	< 5	5-10	--	11-20	21-30
Karyotype	Good	Intermediate	Poor	--	--

Cytopenias	0/1	2/3	--	--	--

Prognosis			
Overall Score	**IPSS Group**	**Median survival (y)**	**25% AML progression (y)**
0	Low	5.7	9.4
0.5-1	Intermediate-1	3.5	3.3
1.5-2	Intermediate-2	1.1	1.1
> 2.5	High	0.4	0.2

Scoring system: A score from 0 to 2 is determined for each of the three variables; the three values are added to obtain the IPSS score. Example, a patient with 12 percent bone marrow blasts (score 1.5), complex chromosomal changes (poor karyotype score 1), neutrophil count of 1000/microL, and platelet count of 50,000/microL (two cytopenias = score 0.5) would have an IPSS score of 3 (= high risk). Patients with 20-30% blasts may be considered to have MDS (FAB) or AML (WHO)
Karyotype-Cytogenetics: [Excludes karyotypes t(8;21), inv16, and t(15;17) which are considered to be AML and not MDS]
Good = normal, -Y alone, del(5q) alone, or del(20q) alone
Poor = complex (≥ 3 abnormalities) or chromosome 7 anomalies
Intermediate = other abnormalities
Cytopenias:
Absolute neutrophil count < 1,800/mcL
Platelets < 100,000 mcL
Hb < 10 g/dL (100 g/L

Revised International Prognostic Scoring System (IPSS-R)							
Prognostic variable	0	0.5	1	1.5	2	3	4
Cytogenetic	Very good	-	Good	-	Intermediate	Poor	Very poor
Bone marrow blasts (%)	≤ 2	-	> 2- < 5	-	5-10	> 10	-
Hemoglobin	≥ 10	-	8- < 10	< 8	-	-	-
Platelets	≥ 100	50- < 100	< 50	-	-	-	-
ANC	≥ 0.8	< 0.8	-	-	-	-	-

Prognosis			
Overall Score	**IPSS-R Group**	**Median survival (y)**	**25% AML progression (y)**
≤ 1.5	Very low	8.8	Not reached
> 1.5- ≤ 3	Low	5.3	10.8
> 3- ≤ 4.5	Intermediate	3	3.2
> 4.5- ≤ 6	High	1.6	1.4
> 6	Very high	0.8	0.7

Cytogenetic risks:
Very good = -Y, del(11q)
Good = normal del(5q), del(12p), del(20q), double including del(5q)
Intermediate = del(7q), +8, +19, i(17q), any single or double independent clones

Poor = -7, inv(3)/t(3q)/del(3q), double including -7/del(7q), complex: 3 abnormalities ***Very poor*** = complex: 3 abnormalities

Performance scores:

Eastern Cooperative Oncology Group (ECOG) Score (also known as Zubrod Score)	
0	Asymptomatic, fully active, able to carry on all pre-disease performance without restriction
1	Symptomatic, fully ambulatory, restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, for example light housework or office work
2	Symptomatic, in bed less than 50% of the day, ambulatory and capable of all self-care but unable to carry out any work activities
3	Symptomatic, confined to bed or chair more than 50% of the day but not bedridden, capable of only limited self-care
4	Bedridden, cannot perform any self-care, completely disabled
5	Dead

Karnofsky Performance Score:	
100%	Able to carry on normal activity, no evidence of disease
90%	Able to carry on normal activity, minor signs or symptoms of disease
80%	Normal activity with effort, some signs and symptoms of disease
70%	Cares for self, unable to carry on normal activity or to work
60%	Requires occasional assistance from others but able to care for most needs
50%	Requires considerable assistance from others and frequent medical care
40%	Disabled, requires special care and assistance
30%	Severely disabled, hospitalization indicated, though death not imminent
20%	Very sick, hospitalization indicated, active support treatment necessary
10%	Moribund
0%	Dead

Lansky Play Score (Also known as Lansky Play - Performance Scale):	
100	Fully active, normal
90	Minor restrictions in physically strenuous activity
80	Active, but tires more quickly
70	Both greater restriction of and less time spent in play activity
60	Up and around, but minimal active play; keeps busy with quieter activities
50	Gets dressed but lies around much of the day, no active play but able to participate in all quiet play and activities
40	Mostly in bed; participates in quiet activities
30	In bed; needs assistance even for quiet play
20	Often sleeping; play entirely limited to very passive activities
10	No play; does not get out of bed
0	Unresponsive

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